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The known unknowns of anomalous trichromacy

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Anomalous trichromacy is the most common minority color vision phenotype, yet the category label obscures a large range of individual differences both in the underlying genetics and in color perception. This review explores both, particularly considering possible reasons for the smaller than expected observed relationship between the spectral sensitivities of anomalous cones and color discrimination. Also considered is the putative process of postreceptoral compensation, where anomalous trichromats may amplify the reduced color signals they receive from their cones to relatively normalize their color vision postreceptorally.

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Anomalous trichromacy is defined by an abnormal Rayleigh match: deuteranomals require more green in a red/green mixture than normal to match an amber primary, while protanomals require more red [1]. Anomalous trichromacy is the most common form of color vision deficiency (CVD), so called because color discrimination is usually (though not always) impaired from normal. Rates of CVD vary somewhat in different populations [2•], but anomalous trichromacy is always more common than dichromacy. In European Caucasians, for example, deuteranomaly affects about 5% of men and protanomaly 1% of men, while deuteranopia and protanopia each affect about 1% of men [3–5].

The discrete labels of deuteranomaly and protanomaly obscure the plethora of individual variation among observers that are defined under each label. In fact, it is helpful to think of deuteranomaly and protanomaly as color vision categories. Starting with the genetic underpinnings of anomalous trichromacy, there is extensive individual variation. Trichromacy occurs when the first two genes in the 'opsin' array at Xq28 differ at one or more of at least seven genomic positions which contribute to variation in the spectral tuning of the L and M opsins [6•]. Normal trichromacy results when the cumulative spectral separation conferred by the spectrally-active polymorphisms exceeds some threshold, probably about 15 nm [7], which is enough to produce a normal Rayleigh match.[1] Anomalous trichromacy results when the spectral separation between the pigments produced by the first two genes in the opsin array is about 12 nm or smaller.[2]

The literature contains many references to 'hybrid' genes, which, by unequal recombination, contain concatenated sections from both M and L opsin genes [8•–11]. On the other hand, there are also many genetic polymorphisms which confer spectral differences between the opsins, but underlie variation in the spectral tuning of the L and M opsins in normal trichromacy [6•,9,12–14]. This difference in language between hybrid genes in anomalous trichromacy and polymorphic genes in normal trichromacy reflects a long-held difference of opinion surrounding the (at the time putative) genetic basis of anomalous color vision [15•]. The protanolabe/deuteranolabe hypothesis [16] proposed that anomalous trichromacy is caused by the presence of hybrid photopigment genes particular to anomalous trichromats which are not part of the opsin gene pool expressed in normal color vision. A competing hypothesis by Alpern and Moeller [17] proposed that anomalous trichromats express two polymorphic versions of 'normal' opsin genes.

Given that much of the variation in opsin genes has been produced by unequal crossing over [6•,11,18], most

[1] In theory, the midpoint of the Rayleigh match depends both on the spectral separation and on the absolute peak sensitivities of the observer's long and medium wavelength sensitive cones [48,77]. For example, an observer could theoretically have a spectral separation typical of anomalous observers of, say, 6nm, yet make a normal match if the two cone types have peak spectral sensitivities on either side of 545 nm (see Figure 1 in [48]). However, variation in the L and M opsin genes groups them two types, L-class and M-class [6•], meaning that the peak spectral sensitivities also tend to fall into two clusters, and thus, observers with spectral separations typical of anomalous observers but with normal Rayleigh midpoints, if they exist at all, are rare.

[2] Although the midpoint of the Rayleigh match may depend both on the peak spectral sensitivities and the spectral separation of the long and medium wavelength sensitive opsins, it is true to say that if an observer has at least one photopigment with a peak sensitivity close to that of the normal L cone or at least one photopigment with a peak sensitivity close to that of the normal M cone, then abnormally reduced spectral separation between the two available long and medium wavelength sensitive cone types is sufficient to confer anomalous trichromacy. Because of the clustering of the long and medium wavelength sensitive cone types into two classes, this is the case in most, if not all, instances of anomalous trichromacy.

polymorphic variants of M or L opsin genes could be considered hybrid because they contain sections from ancestral M and L opsin genes. Both the protanolabe/deuteranolabe hypothesis and the Alpern and Moeller hypothesis turned out to be true, because L and M opsin variants can be considered both polymorphic (differing at locations that confer spectral differences) and hybrid (containing DNA sections from both ancestral M and ancestral L opsin genes). Instead of continuing to talk about hybrids which seems to set the opsin genes of anomalous trichromats apart from those of normal trichromats, it may be more helpful to adopt the language of Neitz, Neitz *et al.* [6•,10] who categorize opsins into two classes (L-class or M-class) depending on the codons present at positions 277 and 285 of exon 5 in the 6-exon opsin gene, because variation at these locations confers 20 nm of the spectral separation between the M and L cones. Certain polymorphisms in exons 2, 3 and 4, which also shift the spectral tuning of the opsins but by a lesser degree, are considered within-class variants.

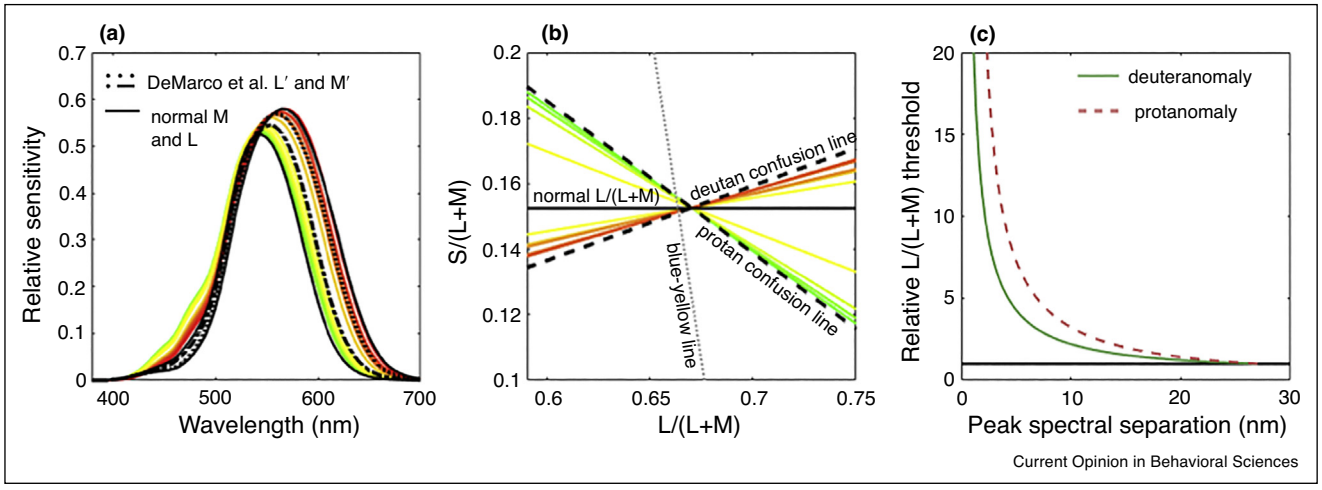
Under this view, deuteranomaly occurs when the expressed M-class gene is replaced by a second L-class gene, while protanomaly occurs when the expressed L-class gene is replaced by a second M-class gene. Accordingly, the opsin genes found in anomalous trichromacy overlap with those found in normal trichromacy [7,19,20], though it is possible that the frequencies of some genotypes are raised in anomalous trichromacy [6•]. It is also possible that there are certain opsin genes that are exclusive to anomalous trichromats: If the expressed opsin's spectral sensitivity is mid-way between that of the normal M and that of the normal L cones it may confer anomalous trichromacy whether it occurs with a normal M opsin gene or with a normal L opsin gene. However, an opsin gene that confers only a small spectral separation with, say, the average peak sensitivity of the normal L opsin, confers deuteranomaly if the other expressed gene in the opsin array is L-class, but confers normal trichromacy (and would be considered a normal polymorphism) if inherited with an M-class opsin gene [for such cases see Ref. 19].

Setting aside this somewhat semantic issue of whether anomalous genes are best considered 'hybrids', over the last three decades, we have gained quite a good understanding of the genetic variations commonly underlying anomalous trichromacy. The genetic cause of anomalous trichromacy remains unaccounted for in only a small number of cases, for example, in rare reports of phenotypic anomalous trichromacy in the presence of normal opsin genes [e.g. Refs. 21,22]. In most cases, the link between variations in genotype and variations in absorption spectra of the opsins has been established by expressing cDNAs *in vitro* and measuring absorption spectra before and after photobleaching [8•,14]. An *in vivo* model of resulting sensitivity functions can created by including corrections for optical density, lens and macular pigment (e.g. see Appendix in Ref. [23]). A selection of modelled cone sensitivity functions for known anomalous genotypes [8•] is shown in Figure 1(a), for comparison with template protanomalous and deuteranomalous cone sensitivity functions by DeMarco *et al.* [24•].

What is the relationship between divergent anomalous genotypes and color vision phenotypes? 'Red/green' color distinctions are made by comparing the activities of the long and medium wavelength sensitive cones. Any genetic mutation that reduces the spectral separation between these two cone types from the normal ~30 nm would be expected to reduce the size of the comparison signal and adversely affect color discrimination. The MacLeod-Boynton [28] chromaticity diagram is a useful way of representing the basic color comparisons that the early visual system makes. Signals from the 'ancient' color subsystem [30] which compares the activity of the S cones to that of the other cone classes is plotted up the ordinate, and signals from the more recently evolved subsystem that compares the activities of the medium and long wavelength sensitive cones is plotted along the abscissa. In this chromaticity diagram, the deuteranopic and protanopic confusion lines emanate from the points $x = y = 0$ and $x = 1$, $y = 0$, respectively [28]. Figure 1(b) and (c) show the results of a model (described in the figure legend) that predicts anomalous color vision based on the different anomalous cone types (with the 'normal' cone type fixed in its spectral sensitivity). Figure 1(b) shows the anomalous equivalents of $L/(L + M)$ color variation through a white point plotted in the normal color space (for a particular set of RGB primaries, note that observer metamerism makes this impossible for arbitrary spectra e.g. Ref. [27]). As the spectral separation between the two medium and long wavelength photopigments reduces, this locus tends away from the horizontal normal $L/(L + M)$ axis towards the deuteranopic confusion lines. Figure 1(c) shows the predicted effect of anomalous cone photopigments on the $L/(L + M)$ color signal that presumably underlies 'red/green' color discrimination: As the spectral separation between the two cone types reduces, roughly exponentially larger color differences are necessary to achieve the same color difference signals, and sensitivity is inversely proportional to these color differences. If color discrimination were perfectly predictable in this way from cone sensitivity functions, then there ought to be a high correlation (moderated by the absolute peak spectral sensitivities depending on the particular spectra) in anomalous trichromacy between the spectral separation of the two medium or long wavelength sensitive opsins predicted from genotype, and color discrimination phenotype.

Empirical color discrimination data shows high individual variability amongst anomalous trichromats, from performance indistinguishable to that of normal trichromats, to

Figure 1



(a) The colored lines show simulated cone sensitivity functions based on the peak sensitivities of expressed 'anomalous' opsins *in vitro* [8•]. The fundamentals are constructed by using a template by Lamb [25], with corrections for optical density, lens and macular pigment. For a more detailed explanation see the appendix to Jordan *et al.* [23]. For comparison, the dotted and dot dash lines show the tabulated anomalous cone sensitivity functions of DeMarco *et al.* [24•], which are modified normal cone sensitivity functions with corrections for optical media (note that these are labelled oppositely than in the DeMarco *et al.* paper to reflect the spectral proximity of each anomalous cone type to the nearest normal cone type, for example, L′ is more similar to L than M). Standard observer L and M cone sensitivity functions given by Smith and Pokorny [26] are shown by the solid black lines. The DeMarco *et al.* [24•] and Smith and Pokorny [26] fundamentals are scaled for comparison with the simulated fundamentals. **(b)** L/(L + M) axes for colors displayed on a HP Dreamcolor LCD monitor for anomalous observers with the simulated cone fundamentals shown in (a). Although it is not possible (because of observer metamerism) to transform arbitrary anomalous cone activities to normal cone activities [e.g. Ref. 27], it is possible to show in the MacLeod-Boynton chromaticity diagram for normal trichromats [28] RGB values (for a given display) that occur at particular positions in an equivalent anomalous chromaticity diagram. The protan and deutan confusion lines are indicated by the labelled dashed lines, and the horizontal normal axis of L/(L + M) variation is shown for comparison. The line from unique blue at 476 nm to unique yellow at 576 [29] nm is shown by the dotted line. As might be expected, as spectral separation decreases in anomalous trichromacy the line of L/(L + M) variation moves away from the line of normal L/(L + M) variation towards the deuteranopic confusion lines. The variation in slope of the L/(L + M) axis for different deuteranomalous observers indicates that any pseudoisochromatic test for CVD may not be effective for anomalous observers whose L/(L + M) axes differ from the confusion lines. However, the difference in slopes between the different L/(L + M) axes and the deuteranopic confusion lines reduces almost to zero when the stimuli to be discriminated elicit little or no S-cone activity. Pseudoisochromatic tests may therefore be effective for more individual observers if constructed around yellow (low S-cone activity) rather than around a neutral grey (higher S-cone activity). **(c)** Predicted discrimination thresholds (relative to a normal threshold of 1) as a function of peak spectral separation between the two medium and long-wavelength sensitive photopigments, for colors varying along the normal L/(L + M) line in Figure 1(b). For the model shown in (b) and (c) the M cone (*in vitro*) peak sensitivity is held constant at 529.7 nm and the L cone peak sensitivity is held constant at 556.7 nm, while the peak sensitivity for the simulated anomalous fundamental varies.

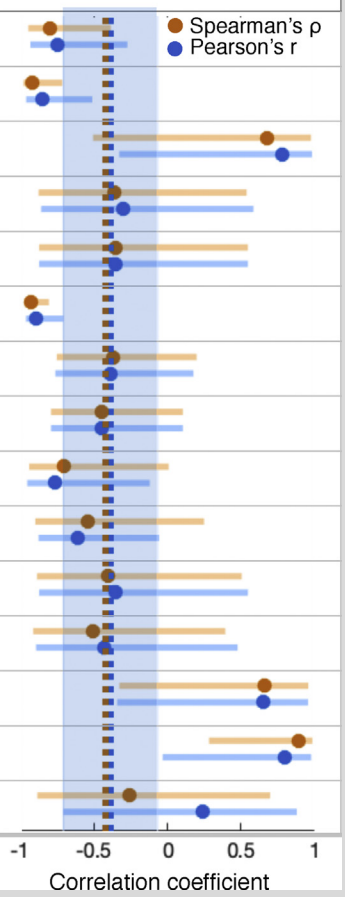
near-dichromatic performance. However, despite a theoretical expectation for a strong relationship between spectral separation and color discrimination, only a small proportion of the variance in empirical data can be accounted for in this way. Table 1 collates reported correlation coefficients for various measures of red/green color sensitivity. The pooled Pearson's r using the Hunter-Schmidt method [36] weighted by n is −0.39, explaining 15.2% of the variability in the data (weighted average Spearman's ρ = −0.42, explaining 17.7% of the variability in ranks). The relationship between the spectral separation of the peak sensitivities of the opsins and color discrimination therefore turns out to be unexpectedly weak, but there are several different factors that may dilute the relationship. First, there is a general absence in the literature of consideration of the reliabilities of the phenotypic measures, meaning that an unknown amount of variance in color discrimination may be attributed to measurement error. Second, there may be specific limitations of the Rayleigh matching range as a measure of color discrimination. Third, there may be biological differences between individuals that could contribute to color discrimination performance independent of the difference between the spectral peaks of the opsin sensitivity functions. I will discuss each of these contentions below.

Measurement error. As for any correlation, the ceiling correlation coefficient for the relationship between opsin genotype and color sensitivity is limited by the test-retest reliabilities of both measures [e.g. Ref. 37]. Though we might assume that (despite the difficulties of genotyping regions with high homology) genotype is highly reliable, we cannot make the same assumption for the phenotypic measures of color sensitivity. What are the reliabilities of the measures of color discrimination listed in Table 1? Evaluation of tests for CVD prioritises sensitivity and

Table 1

Correlation between spectral separation and sensitivity to red-green color differences [31•,32–35].

Reference and discrimination test	Deutan/ protan	Spearman's ϱ	Pearson's r	n	Meta-analysis
Barbur et al. (2008) Nagel matching range [31]	D	-0.80	-0.75	11	
Barbur et al. (2008) Red-green CAD units [31]	D	-0.92	-0.85	11	
Crognale et al. (1998) small field matching range [32]	D	0.68	0.78	5	
Crognale et al. (1998) large field matching range [32]	D	-0.36	-0.3	7	
Jordan et al. (2010) matching range [23]	D	-0.35	-0.35	7	
Neitz et al. (1996) AO-HRR [10]	D	-0.93	-0.89	16	
Sanocki et al. (1997) small field matching range [33]	D	-0.37	-0.39	14	
Sanocki et al. (1997) large field matching range [33]	D	-0.45	-0.45	14	
Shevell et al. (1998) matching range [34]	D	-0.70	-0.76	8	
Deeb et al. (1993) matching range [35]	D	-0.54	-0.61	12	
Crognale et al. (1998) large field matching range [32]	P	-0.4	-0.35	7	
Crognale et al. (1998) small field matching range [32]	P	-0.51	-0.43	7	
Sanocki et al. (1997) small field matching range [33]	P	0.66	0.65	6	
Sanocki et al. (1997) large field matching range [33]	P	0.89	0.80	6	
Deeb et al. (1993) matching range [35]	P	-0.26	0.24	6	



N.B. Participants who are genetically or phenotypically dichromatic were excluded.

specificity for assigning diagnostic categories (in many cases as basic as CVD versus normal) rather than measuring within-category individual differences, and I have identified only two studies that have assessed the test-retest reliability of matching range. Anderson and Johnston [38] reported a test-retest reliability of r = 0.7 (ρ = 0.49, from their Figure 1d) in 32 normal trichromats. For 7 deuteranomals, data from Geri and Neri [39] show a test-retest reliability of only r = 0.26 (ρ = 0.14), though this is for the solid state Kintz anomalscope rather than for more conventional models (e.g. Nagel). Though the available data are scant, because the measures of color discrimination typically used are not designed to discriminate within-category individual differences, we may reasonably assume that test-retest reliabilities for this purpose are relatively low. Low reliabilities will place a corresponding low ceiling on the expected relationship between genotype and color discrimination.

Validity of the Rayleigh matching range as a measure of color discrimination. A high correlation between opsin genotype and color sensitivity also relies on the validity of the color sensitivity measure. Because the tests listed in Table 1 are designed to diagnose color vision phenotype, they do not necessarily also constitute valid tests for within-category individual differences in color sensitivity. Evidently they have some capacity for the latter purpose, since there is a relationship between matching range and genotype, both in anomalous trichromats (Table 1) and normal trichromats [13•]. Nonetheless, there is good reason to doubt the validity of matching range in particular as a measure of within-group color sensitivity. Several authors have pointed out that matching range, as a yes-no task, is prone to criterion biases (both among observers and among experimenters) which can have a large impact on results [38,40•–42], and adaptation to the test field is known to contribute to variability in matching range via individual differences in rates of adaptation to the test field and by variation in test field presentation time [43]. When the method of administering the anomaloscope is altered into a forced-choice psychophysical procedure, matching ranges tend to reduce substantially [41]. It is

notable that the two measures of color sensitivity other than matching range listed in Table 1 show strong correlations with genotype, explaining an average of 86% of the variation — perhaps this is because they are more valid and/or reliable measures of color discrimination than matching range.

Individual variations independent of the spectral separation of the opsins. One factor which will somewhat dilute the relationship between spectral separation and color discrimination is the absolute peak sensitivities of the photopigments, yet in most published predictions of anomalous color discrimination, the peak sensitivity of one of the two cone fundamentals tends to be fixed [e.g. Refs. [44•–46•]. Though the influence of the absolute peak sensitivities of all three photopigments is specific to the particular stimulus spectra, and small compared to the influence of spectral separation, it is worth including as an additional variable in predictions of anomalous color discrimination. Other than the spectral sensitivities of the photopigments, the individual difference most commonly proposed to affect color discrimination in anomalous trichromacy is variation in optical density [15•,44•,45,47•,48]. Increasing optical density tends to broaden a cone's spectral sensitivity function. Therefore, if the two medium or long wavelength-sensitive photopigments expressed in the retina of an anomalous trichromat differ in optical density, color vision tends to be enhanced because the overall spectral overlap between the two cone sensitivity functions tends (depending on the particular peak sensitivities) to be reduced [44•,45,47•]. Though this idea remains largely a theoretical possibility, it has been rendered more likely by the presence, correlated with genetic variation in exon 2 of the M and L opsin gene, of anomalous trichromacy without genes for two spectrally distinct opsins [22,49], and by an up to 3 nm variation in peak spectral sensitivity measured psychophysically in dichromats with shared genotypes [50]. Other than optical density there are further uninvestigated variations that could confer differences in color discrimination among anomalous trichromats. For instance, Broackes [51•] has proposed that individuals with CVD may be able to make use of dynamic color signals provided by changing illumination, or dynamic signals caused by eye movements as colored light passes through different densities of macular pigment. There may be varying input to chromatic channels from rods [52–54] or IPRGs [55]. Chromatic aberration may provide a color signal [56]. All of these possible sources of color information may be better utilised by some individuals than by others. Finally, there may be individual differences in the degree of *postreceptoral compensation* [57•,58] for the reduced color comparison signals encoded by the retinae of anomalous trichromats (see below for an elaborated discussion of this possibility). If postreceptoral compensation occurs upstream of the performance limiting source of noise then it would be expected to impact color discrimination.

Since Rayleigh match midpoint, matching range and peak spectral separation of the long and medium wave cone fundamentals all depend on differences in genotype, relationships are also expected between peak spectral separation and match midpoint (positive for deuteranomals and negative for protanomals), and between midpoint and matching range (negative for deuteranomals and positive for protanomals). However, the observed relationships are even weaker than the observed relationships between spectral separation and color discrimination recorded in Table 1. For midpoint and spectral separation, the weighted average correlation for deuteranomals from a number of studies listed in Table 2 is $r = -0.13$ ($\rho = -0.24$). For midpoint and range the weighted average correlation is $r = 0.13$ ($\rho = 0.06$) for deuteranomals and $r = -0.30$ ($\rho = -0.31$) for protanomals. But why are the observed relationships weak and statistically non-significant? One obvious reason is the direct dependence of midpoint on range. Since midpoint is simply the center of the matching range, there is no guarantee that it constitutes the 'best' (i.e. average) match [42]. Midpoint is also as prone to observer and experimenter criterion biases as matching range. If the Rayleigh match were administered as a performance-based psychophysical task [23,40•,41] and the 'midpoint' redefined as the point of minimum ability to discriminate the mixture from reference fields, then 'midpoint' would be a more meaningful measure, and its relationships with spectral separation and color sensitivity would likely be stronger. Additionally, the same multitude of factors (discussed above) that weaken the relationship between sensitivity and peak spectral separation will also weaken the relationship between midpoint and range.

Potentially separate from the impact of anomalous trichromacy on color sensitivity is its impact on color appearance. Though many studies lack the necessary (anomaloscope) data to confidently classify participants with CVD into anomalous trichromats and dichromats, three studies which did isolate anomalous trichromacy found increased errors in color naming tasks for basic color categories [63–65], indicating an impact on color appearance. Color appearance in anomalous trichromacy has also been addressed psychophysically, by asking participants to assign ratings of color dissimilarities among a set of stimuli and then using multidimensional scaling to reconstruct estimates of the perceptual color spaces used by participants to assign the ratings [66]. Results typically show a relative contraction in the representation of color differences that rely on signals from the medium and long wavelength sensitive cones [67,68•,69], though in some cases there can be a relative *expansion* in perceptual color space if particular stimuli are chosen that are predicted to be close to metameric for a normal trichromatic observer

Table 2

Correlation between spectral separation and Rayleigh match midpoint and between midpoint and range [59,60*,61,62].

Reference and discrimination test	Deutan/ protan	Spearman's ϱ	Pearson's r	n	Meta-analysis
Relationship between Rayleigh match midpoint and spectral separation					Spearman's ρ Pearson's r
Barbur et al. (2008) [31]	D	-0.02	0.19	11	
Jordan et al. (2010) [23]	D	0.08	0.04	7	
Sanocki et al. (1997) small field [33]	D	-0.40	-0.37	14	
Sanocki et al. (1997) large field [33]	D	-0.67	-0.46	14	
Shevell et al. (1998) [34]	D	0.22	0.27	8	
Sanocki et al. (1997) small field [33]	P	0.60	0.68	6	
Sanocki et al. (1997) large field [33]	P	0.20	0.01	6	
					-1 -0.5 0 0.5 1 Correlation coefficient
Relationship between Rayleigh match midpoint and range					
Barbur et al. (2008) [31]	D	0.24	0.28	11	
Jordan et al. (2010) Figure 2 [23]	D	0.18	0.42	31	
Sanocki et al. (1997) small field [33]	D	-0.83	-0.81	6	
Sanocki et al. (1997) large field [33]	D	-0.03	0.15	6	
Deeb et al. (1992) [22]	D	0.12	0.47	21	
Shevell et al. (1998) [34]	D	0.31	0.11	8	
Shinomori et al. (2016) [59]	D	-0.28	-0.25	22	
Rodriguez-Carmona and Barbur (2017) [60]	D	0.03	0.08	83	
Willis and Farnsworth (1952) in Hurvich (1972) [61]	D	0.16	0.14	60	
Jordan et al. (2010) Figure 2 [23]	P	0.48	0.72	8	
Deeb et al. (1992) [22]	P	-0.3	-0.74	5	
Shinomori et al. (2016) [59]	P	-0.89	-0.96	6	
Rodriguez-Carmona and Barbur (2017) [60]	P	-0.49	-0.40	23	
Willis and Farnsworth (1952) in Hurvich (1972) [61]	P	-0.20	-0.29	12	
					-1 -0.5 0 0.5 1 Correlation coefficient

N.B. A positive correlation between mid-point and range is expected for protans, but a negative one for deutans.
*Extreme anomalous trichromats removed from the original sample.

Figure 2

Simulation of color appearance in deuteranomaly based on signals sent by anomalous cones of different spectral sensitivities, with most genotypes from Merbs and Nathans [8•]. On each panel are the *in vitro* peak spectral sensitivities of the long and medium wavelength sensitive opsins used for each simulation.

[70•]. There have not been any systematic studies of the relationship between genotype and color appearance in anomalous trichromacy, though several authors have noticed that the degree of difference from normal is related to the degree of CVD. It is possible to model the expected effect of genotype on color appearance (e.g. Refs. [71,72] and Figure 2), but there are good reasons to expect such models may be a poor fit to reality. As well as the individual variations that might affect color discrimination discussed above, there are two ways in which color appearance for anomalous trichromats may be less different to normal than models based on the activities of the cones predict. First, anomalous trichromats may escape some of the compressive nonlinearity in the normal encoding of color saturation postreceptorally [73]. Second, postreceptoral compensation, or the posreceptoral amplification of reduced color signals encoded by the retina might relatively normalise color appearance. One recent model of color appearance in anomalous trichromacy [74] applies postreceptoral compensation (adaptation) to the reduced color contrasts predicted in anomalous trichromacy. The result is almost indistinguishable from normal color appearance. But how plausible an idea is postreceptoral compensation?

The possibility of postreceptoral compensation in anomalous trichromacy was first made explicit by Regan and Mollon [57•] (though was implied much earlier in [75]), who proposed that the signals sent by the 'residual' middle-long wavelength sensitive color channel might 'expand to fill the neural space available', matching the range of color variation to the available dynamic range of visual neurons. They tested this idea by measuring the relative saliences of the signals from the two cardinal color mechanisms. Although they found that for most anomalous trichromats the relative salience of differences in L/(L + M) compared to differences in S/(L + M) was reduced (from normal) by a factor of 3–5, there were two individual anomalous trichromats for whom this relative salience seemed normal. Boehm *et al.* [46•] compared, in the same anomalous trichromats, color discrimination at threshold, with a suprathreshold measure of color perception constructed using multidimensional scaling. In 9 deuteranomals, color discrimination thresholds were raised from normal by an average factor of 2.6, which was broadly in line with (though somewhat better than) a prediction based on reduced spectral separations between the M and L photopigments. However, suprathreshold, the range of perceived color differences along the L/(L + M) axis in the reconstructed color spaces was contracted by a factor of only 1.16 from normal, much less than predicted from the model. The results of both studies are compatible with the idea of postreceptoral compensation, though Boehm *et al.'s* results indicate that it is the norm, rather than being isolated to a minority of anomalous trichromats. The difference between Boehm

et al.'s results at threshold and suprathreshold imply that most of the postreceptoral compensation occurs downstream of the source of noise that limits color discrimination performance. However, a difference between predicted and observed thresholds leaves open the possibility of some level of compensation upstream of the noise that limits color discrimination, if the difference is not explained by other factors like optical density discussed above. For postreceptoral compensation that is specific to suprathreshold color differences, it is, however, difficult in behavioural experiments to rule out a strategy of 'cognitive compensation', where reduced color differences are cognitively relabelled, rather than lower-level perceptual compensation. The next step in research into postreceptoral compensation must look at direct measures of brain activity to try to isolate the process to visual regions of the brain. Such studies are currently being attempted: Initial fMRI measurements in anomalous trichromats viewing L/(L + M) gratings show evidence of postreceptoral compensation in early visual areas, with the degree of compensation varying between individuals [76•].

In conclusion, although the genetic bases of individual differences in the ability to discriminate medium and long wavelength light are relatively well understood compared to those of other individual differences in visual perception, there remain a number of unsolved mysteries. Color discrimination in anomalous trichromats shows wide individual variation, ranging from as good as that of normal trichromats to near deuteranopic. Only a small proportion of the individual variation has so far been attributed to differences in genotype (though the proportion might rise with more reliable and valid measures of color discrimination), and suggestions for additional individual differences that might explain variation in color discrimination are interesting but have not been empirically verified. Color differences for anomalous trichromats are reduced from normal along the L/(L + M) axis in the MacLeod-Boynton [28] chromaticity diagram, but the difference in suprathreshold color appearance from normal seems to be much less than is predicted from the increased spectral overlap of the medium and long wavelength sensitive cones. Postreceptoral compensation, predominantly downstream of the principal source of noise that limits color discrimination, seems the best explanation for the limited available data, though its mechanisms are as yet poorly understood.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest

1. Franceschetti A: **Die Bedeutung der Einstellungsbreite am Anomaloskop für die Diagnose der eizelnen Typen der Farbensinnstörungen nebst Bemerkungen uber ihre Vererbungsmodus**. *Swiss Med Wkly* 1928, **52**:1273-1278.
2. • Birch J: **Worldwide prevalence of red-green color deficiency**. *J Opt Soc Am A* 2012, **29**:313.
3. Birch J: **Classification of anomalous trichromatism with the Nagel anomaloscope**. In *Colour Vision Deficiencies XI*. Edited by Drum B. Springer Science+Business Media; 1991:13-18.
4. Birch J: **Identification of red-green colour deficiency: sensitivity of the Ishihara and American Optical Company (Hard, Rand and Rittler) pseudo-isochromatic plates to identify slight anomalous trichromatism**. *Ophthal Physiol Opt* 2010, **30**:667-671.
5. Sharpe LT, Stockman A, Jägle H, Nathans J: **Opsin genes, cone photopigments, color vision, and color blindness**. In *Color vision, from genes to perception*. Edited by Gegenfurtener K, Sharpe L. Cambridge University Press; 1999:3-51.
6. • Neitz J, Neitz M: **The genetics of normal and defective color vision**. *Vis Res* 2011, **51**:633-651.
7. Davidoff C: *Cone opsin gene variants in color blindness and other vision disorders*. 2015.
8. • Merbs SL, Nathans J: **Absorption spectra of the hybrid pigments responsible for anomalous color vision**. *Science* 1992, **258**:464-466.
9. Deeb SS: **The molecular basis of variation in human color vision**. *Clin Genet* 2005, **67**:369-377.
10. Neitz J, Neitz M, Kainz PM: **Visual pigment gene structure and the severity of color vision defects**. *Science (80-)* 1996, **274**:801-804.
11. Hunt DM, Carvalho LS: **The genetics of color vison and congenital color deficiencies**. In *Human Color Vision*. Edited by Kremers J, Marshall NJ, Baraas RC. Springer; 2016:1-32.
12. Merbs SL, Nathans J: **Absorption spectra of human cone pigments**. *Nature* 1992, **356**:433-435.
13. • Winderickx J, Lindsey DT, Sanocki E, Teller DY, Motulsky AG, Deeb SS: **Polymorphism in red photopigment underlies variation in colour matching**. *Nature* 1992, **356**:431-433.
14. Asenjo AB, Rim J, Oprian DD: **Molecular determinants of human red/green color discrimination**. *Neuron* 1994, **12**:1131-1138.
15. • Mollon JD: **" . . . aus dreyerley Arten von Membranen oder Molekülen": George Palmer's legacy**. In *Colour Vision Deficiencies XIII*. Edited by Cavonius CR. Springer; 1995:3-21.
16. Rushton WAH: **Pigments in anomalous colour vision**. *Vis Res* 1973, **13**:2017-2031.
17. Alpern M, Moeller J: **The red and green cone visual pigments of deuternomalous trichromacy**. *J Physiol* 1977, **266**:647-675.
18. Winderickx J, Battisti L, Hibiya Y, Motulsky AG, Deeb SS: **Haplotype diversity in the human red and green opsin genes: Evidence for frequent sequence exchange in exon 3**. *Hum Mol Genet* 1993, **2**:1413-1421.
19. Neitz M, Neitz J, Grishok A: **Polymorphism in the number of genes encoding long-wavelength-sensitive cone pigments among males with normal color vision**. *Vis Res* 1995, **35**:2395-2407.
20. Sharpe LT, Stockman A, Jägle H, Knau H, Klausen G, Reitner A, Nathans J: **Red, green, and red-green hybrid pigments in the human retina: correlations between deduced protein sequences and psychophysically measured spectral sensitivities**. *J Neurosci* 1998, **18**:10053-10069.
21. Davidoff C, Neitz M, Neitz J: **Genetic testing as a new standard for clinical diagnosis of color vision deficiencies**. *Transl Vis Sci Technol* 2016, **5**:2.
22. Deeb SS, Lindsey DT, Hibiya TY, Sanocki E, Winderickx J, Teller DY, Motulsky AG: **Genotype-phenotype relationships in human red/green color-vision defects : molecular and psychophysical studies**. *Am J Hum Genet* 1992, **51**:687-700.
23. Jordan G, Deeb SS, Bosten JM, Mollon JD: **The dimensionality of color vision in carriers of anomalous trichromacy**. *J Vis* 2010, **10**:12.

24. • DeMarco P, Pokorny J, Smith VC: **Full-spectrum cone sensitivity functions for X-chromosome-linked anomalous trichromats**. *J Opt Soc Am A* 1992, **9**:1465-1476.

25. Lamb TD: **Photoreceptor spectral sensitivities: common shape in the long-wavelength region**. *Vis Res* 1995, **35**:3083-3091.

26. Smith VC, Pokorny J: **Spectral sensitivity of the foveal cone photopigments between 400 and 500 nm**. *Vis Res* 1975, **15**:161-171.

27. Knoblauch K: **Representing an observer's matches in an alien colour space**. In *Normal and Defective Colour Vision.* Edited by Mollon JD, Pokorny J, Knoblauch K. Oxford University Press; 2003:267-272.

28. MacLeod DI, Boynton RM: **Chromaticity diagram showing cone excitation by stimuli of equal luminance**. *J Opt Soc Am* 1979, **69**:1183-1186.

29. Mollon J: **Monge: the Verriest lecture, Lyon, July 2005**. *Vis Neurosci* 2006, **23**:297-309.

30. Regan BC, Julliot C, Simmen B, Viénot F, Charles-Dominique P, Mollon JD: **Fruits, foliage and the evolution of primate colour vision**. *Philos Trans R Soc B Biol Sci* 2001, **356**:229-283.

31. • Barbur JL, Rodriguez-Carmona M, Harlow JA, Mancuso K, Neitz J, Neitz M: **A study of unusual Rayleigh matches in deutan deficiency**. *Vis Neurosci* 2008, **25**:507-516.

32. Crognale MA, Teller DY, Motulsky AG, Deeb SS: **Severity of color vision defects: electroretinographic (ERG), molecular and behavioral studies**. *Vis Res* 1998, **38**:3377-3385.

33. Sanocki E, Teller DY, Deeb SS: **Rayleigh match ranges of red/green color-deficient observers: psychophysical and molecular studies**. *Vis Res* 1997, **37**:1897-1907.

34. Shevell SK, He JC, Kainz P, Neitz J, Neitz M: **Relating color discrimination to photopigment genes in deutan observers**. *Vis Res* 1998, **38**:3371-3376.

35. Deeb SS, Winderickx J, Motulsky AG: **Correlation between Rayleigh match range in protans and deutans and the difference in λ_{max} between hybrid and normal pigments**. In *Colour Vision Deficiencies XII.* Edited by Drum B. Springer; 1993:119-126.

36. Hunter JE, Schmidt FL: *Methods of Meta-analysis*. Sage Publications; 2004.

37. Mollon JD, Bosten JM, Peterzell DH, Webster MA: **Individual differences in visual science : what can be learned and what is good experimental practice?** *Vis Res* 2017, **141**:4-15.

38. Anderson AJ, Johnston AW: **Test/retest and inter-test agreement of color aptitude measures**. *Color Res Appl* 2015, **40**:224-231.

39. Geri GA, Neri DF: **Validation of a solid-state anomaloscope used to assess red-green color vision defects**. *Behav Res Methods Instrum Comput* 1988, **20**:27-31.

40. • Stillman JA: **Psychophysical influences on the validity of anomaloscopic assessments of color vision**. *Percept Psychophys* 2008, **70**:1243-1247.

41. Swanson WH: **Analysis of Rayleigh match data with psychometric functions**. *J Opt Soc Am A* 2008, **10**:1807.

42. Humanski RA, Shevell SK: **Factors contirbuting to differences in Rayleigh matches of normal trichromats**. In *Colour Vision Deficiencies X.* Edited by Drum B, Moreland JD, Serra A. Kluwer Academic Publishers; 1991:273-283.

43. Cohen JD, Greenbaum HB: **Asthenopia in normal and red–green color deficient observers**. In *Colour vision deficiencies VI..* Edited by Verriest G. Dr. D.W. Junk Publishers; 1982:79-85.

44. • Shevell SK, He JC: **Phenotypes of anomalous trichromacy**. In *Colour Vision Deficiencies XIII.* Edited by Cavonius CR. Springer; 1997:44-58.

45. He JC, Shevell SK: **Variation in color matching and discrimination among deuteranomalous trichromats: theoretical implications of small differences in photopigments**. *Vis Res* 1995, **35**:2579-2588.

46. • Boehm AE, MacLeod DIA, Bosten JM: **Compensation for red-green contrast loss in anomalous trichromats**. *J Vis* 2014, **14** 19–19.

47. • Thomas PBM, Formankiewicz MA, Mollon JD: **The effect of photopigment optical density on the color vision of the anomalous trichromat**. *Vis Res* 2011, **51**:2224-2233.

48. Thomas PBM, Mollon JD: **Modelling the Rayleigh match**. *Vis Neurosci* 2004, **21**:477-482.

49. Neitz J, Neitz M, He JC, Shevell SK: **Trichromatic color vision with only two spectrally distinct photopigments**. *Nat Neurosci* 1999, **2**:884-888.

50. Sharpe LT, Stockman A, Jägle H, Knau H, Klausen G, Reitner A, Nathans J: **Red, green, and red-green hybrid pigments in the human retina: correlations between deduced protein sequences and psychophysically measured spectral sensitivities**. *J Neurosci* 1998, **18**:10053-10069.

51. • Broackes J: **What do the color-blind see?** In *Color Ontology and Color Science.* Edited by Cohen J, Matthen M. MIT Press; 2010:291-406.

52. Reitner A, Sharpe LT, Zrenner E: **Is colour vision possible with only rods and blue-sensitive cones?** *Nature* 1991, **352**:798-800.

53. Ruddock KH: **Parafoveal colour vision responses of four dichromats**. *Vis Res* 1971, **11**:143-156.

54. Zele AJ, Cao D: **Vision under mesopic and scotopic illumination**. *Front Psychol* 2015, **6**:1-15.

55. Zele AJ, Feigl B, Adhikari P, Maynard ML, Cao D: **Melanopsin photoreception contributes to human visual detection, temporal and colour processing**. *Sci Rep* 2018, **8**:1-10.

56. Stubbs AL, Stubbs CW: **Spectral discrimination in color blind animals via chromatic aberration and pupil shape**. *Proc Natl Acad Sci U S A* 2016, **113**:8206-8211.

57. • Regan BC, Mollon JD: **The relative salience of the cardinal axes of colour space in normal and anomalous trichromats**. In *Colour Vision Deficiencies XIII.* Edited by Cavonius CR. Kluwer; 1997:261-270.

58. MacLeod D: **Colour discrimination, colour constancy and natural scene statistics**. In *Normal and Defective Colour Vision.* Edited by Mollon JD, Pokorny J, Knoblauch K. Oxford University Press; 2003:189-217.

59. Shinomori K, Panorgias A, Werner JS: **Discrimination thresholds of normal and anomalous trichromats: model of senescent changes in ocular media density on the Cambridge Colour Test**. *J Opt Soc Am A* 2016, **33**:A65.

60. • Rodriguez-Carmona M, Barbur JL: **Variability in normal and defective colour vision: consequences for occupational environments**. In *Colour Design.* Edited by Best J. Elsevier Science and Technology; 2017:43-97.

61. Willis MP, Farnsworth D: **Comparative evaluation of anomaloscopes**. *US Naval Submarine Medical Research Laboratory Report 190*. 1952.

62. Hurvich LM: **Color vision deficiencies**. In *Handbook of Sensory Physiology VII/4.* Edited by Jameson D, Hurvich LM. Springer-Verlag; 1972:582-624.

63. Cole BL, Lian KY, Lakkis C: **Using clinical tests of colour vision to predict the ability of colour vision deficient patients to name surface colours**. *Ophthal Physiol Opt* 2007, **27**:381-388.

64. Nagy BV, Németh Z, Samu K, Ábrahám G: **Variability and systematic differences in normal, protan, and deutan color naming**. *Front Psychol* 2014, **5**:1-7.

65. Smith VC, Pokorny J, Swartley R: **Continuous hue estimation of brief flashes by deuteranomalous observers**. *Am J Psychol* 1973, **86**:115-131.

66. Shepard R: **The analysis of proximities: multidimensional scaling with an unknown distance function. II**. *Psychometrika* 1962, **27**:219-246.

67. Müller M, Cavonius C, Mollon J: **Construcing the color space of the deuteranomalous observer**. In *Color Vision Deficiencies X.* Edited by Drum B, Moreland JD. A S. Springer; 1991:377-387.

68. • Paramei GV, Cavonius CR: **Color spaces of color-normal and color-abnormal observers reconstructed from response times and dissimilarity ratings**. *Percept Psychophys* 1999, **61**:1662-1674.

69. Helm CE: **Multidimensional ratio scaling analysis of perceived color relations**. *J Opt Soc Am* 1964, **54**:256-262.

70. • Bosten JM, Robinson JD, Jordan G, Mollon JD: **Multidimensional scaling reveals a color dimension unique to "color-deficient" observers**. *Curr Biol* 2005, **15**:R950-2.

71. Machado GM, Oliveira MM, Fernandes LAF: **A physiologically-based model for simulation of color vision deficiency**. *IEEE Trans Vis Comput Graph* 2009, **15**:1291-1298.

72. Yaguchi H, Luo J, Kato M, Mizokami Y: **Computerized simulation of color appearance for anomalous trichromats using the multispectral image**. *J Opt Soc Am A* 2018, **35**:B278.

73. Robinson A, MacLeod DIA: **The strength of the McCollough effect does not increase linearly with saturation: implications for the cortical color code**. *J Vis* 2011, **11** 344–344.

74. Webster MA, Tregillus KEM: **Visualizing visual adaptation**. *J Vis Exp* 2017, **122**:e54038 http://dx.doi.org/10.3791/54038.

75. Pokorny J, Smith VC: **Evaluation of single-pigment shift model of anomalous trichromacy**. *J Opt Soc Am* 1977, **67**:1196-1209.

76. • Tregillus KEM: *Thesis: Color perception in anomalous trichromats: Neuroimaging investigations of neural compensation for losses in spectral sensitivity*. 2017.

77. Li Z, Carroll J: **An analytical model of the influence of cone sensitivity and numerosity on the Rayleigh match**. *J Opt Soc Am A* 2016, **33**:A228.